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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/914,239	12/04/2001	Maria Pia Protti	9369 V/vmf	1842

466 7590 04/20/2005

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EXAMINER	
DAVIS, MINH TAM B	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 04/20/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/914,239	PROTTI ET AL.	
	Examiner	Art Unit	
	MINH-TAM DAVIS	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 December 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9* is/are pending in the application.

4a) Of the above claim(s) *2 and 6-9* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 3-5* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *08/23/01*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's election with traverse of group I, Claims 1, 3-5, the peptide of SEQ ID NO:10, in Paper of 12/27/04 is acknowledged and entered.

Claims 1-9 are pending in the instant application and Claims 2, 6-9 have been withdrawn from further consideration by the Examiner under 37 CFR 1.142(b) as being drawn to non-elected invention.

Claims 1, 3-5, the species peptide of `SEQ ID NO:10 are currently under prosecution. The species peptides of SEQ ID NO:1-9, 11 are withdrawn from consideration, as being drawn to non-elected inventions.

The traversal is on the following ground(s):

1) The Office does not explain why, applying the identical legal standard to the identical claims, the opposite result is now being reached in the present US national phase application relative to the international application.

2) Applicant submits the translation of the priority document Italian MI99A000396 filed on 01/26/1999. Applicant asserts that all the cited publications are after the priority date.

The submission of the translation of the priority document Italian MI99A000396 filed on 01/26/1999 is acknowledged, and the priority date of the instant application is determined to be 01/26/1999, the filing date of the priority document Italian MI99A000396.

The arguments have been considered but are found not to be persuasive for the following reasons:

This unity of this application clearly does not exist, according to the PCT rule 13.2, because the shared same or corresponding technical feature is not a contribution over the two cited priort arts, which have priority date before the claimed priority date of 01/26/1999. The claimed priority date of US 5,965,535 is 09/12/1997. The claimed priority date of US 20040053822A1 is 03/05/1993 (08/027146).

The requirement is still deemed proper and is therefore made FINAL.

Accordingly, Claims 1, 3-5, the species peptide of `SEQ ID NO:10 are currently under prosecution. The species peptides of SEQ ID NO:1-9 are withdrawn from consideration, as being drawn to non-elected inventions.

OBJECTION

Claims 1, 3-5 are objected to, because it is not clear whether claim 1 is drawn to peptides "comprising" or "consisting" of the groups selected from the group consisting of SEQ ID Nos 1-11.

For the purpose of compact prosecution, it is assumed that claim 1 is drawn to a peptide binding MHC molecule "comprising" SEQ ID No:10.

It is noted only the elected species SEQ ID NO:10 is examined here.

REJECTION UNDER 35 USC 101

35 U.S.C. §101 states:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful

improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

1. Claim 1 is rejected under 35 USC 101 because the claimed invention is directed to non-statutory subject matter.

Claim 1, as written, does not sufficiently distinguish over peptides as they exist naturally because the claim does not particularly point out any non-naturally occurring differences between the claimed products and the naturally occurring products. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. *See Diamond v. Chakrabarty*, 447 U.S. 303, 206 USPQ 193 (1980). The claim should be amended to indicate the hand of the inventor, e.g., by insertion of "Isolated" or "Purified". See MPEP 2105.

REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, WRITTEN DESCRIPTION

The instant specification does not contain a written description of the invention in such full, clear, concise, and exact terms or in sufficient detail that one skilled in the art can reasonably conclude that applicant had possession of the claimed invention at the time of filing.

Claims 1, 3-5 are rejected under 35 USC 112, first paragraph, as lacking an adequate written description in the specification.

Claims 1, 3-5 are drawn to:

Peptide binding MHC class II molecule, SEQ ID No: 10 (claim 1),

A pharmaceutical composition comprising said peptide with pharmaceutically acceptable excipients (claim 3),

A composition of claim 3, further comprising one or more peptides binding MHC class I molecules corresponding to CTL CD8+ epitopes (claim 4), and

A composition of claim 3 for use as a vaccine (claim 5).

For the purpose of compact prosecution, it is assumed that claim 1 is drawn to a peptide binding MHC molecule "comprising" SEQ ID No:10.

Claims 1, 3-5 encompass unknown sequences attached to SEQ ID NO:10.

Although drawn to DNA arts, the findings in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997) and Enzo Biochem, Inc. V. Gen-Probe Inc. are relevant to the instant claims. The Federal Circuit addressed the application of the written description requirement to DNA-related inventions in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). The court stated that A [a] written description of an invention involving a chemical genus, like a description of a chemical species, requires a precise definition, such as by structure, formula, [or] chemical name, of the claimed subject matter sufficient to distinguish it from other materials.Id. At 1567, 43 USPQ2d at 1405. The court also stated that

> a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA" without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed

> by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is.

Id. At 1568, 43 USPQ2d at 1406. The court concluded that "naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material." Id.

Finally, the court addressed the manner by which a genus of cDNAs might be described. "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." Id.

The Federal Circuit has recently clarified that a DNA molecule can be adequately described without disclosing its complete structure. See Enzo Biochem, Inc. V. Gen-Probe Inc., 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002). The Enzo court adopted the standard that the written description requirement can be met by "show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics ....i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed

correlation between function and structure, or some combination of such characteristics. " Id. At 1324, 63 USPQ2d at 1613 (emphasis omitted, bracketed material in original).

The inventions at issue in Lilly and Enzo were DNA constructs per se, the holdings of those cases are also applicable to claims such as those at issue here.

Thus, the instant specification may provide an adequate written description of a peptide comprising SEQ ID NO:10, as shown in the example of Lilly by structurally describing a representative number of peptide comprising SEQ ID NO:10, or by describing "structural features common to the members of the genus, which features constitute a substantial portion of the genus." Alternatively, as shown in the example of Enzo, the specification can show that the claimed invention is complete "by disclosure of sufficiently detailed, relevant identifying characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics.

In this case, the specification does not describe a peptide comprising SEQ ID NO:10 in a manner that satisfies either the standards as shown in the example of Lilly or Enzo. The specification does not provide the complete structure of any peptide comprising SEQ ID NO:10, other than MAGE-3 comprising SEQ ID NO:10, nor any physical or chemical characteristics of a peptide comprising SEQ ID NO:10, other than MAGE-3 comprising SEQ ID NO:10, nor any functional characteristics coupled with a known or disclosed correlation between structure and function. Although the specification discloses MAGE-3 comprising SEQ ID NO:10, this does not provide a

description of a peptide comprising SEQ ID NO:10, that would satisfy the standard as shown in the example of Enzo.

The specification also fails to describe a peptide comprising SEQ ID NO:10, by the example in Lilly. The specification describes only a single MAGE-3 comprising SEQ ID NO:10. Therefore, it necessarily fails to describe a representative number of such species. In addition, the specification also does not describe "structural features common to the members of the genus, which features constitute a substantial portion of the genus." One of skill in the art would conclude that Applicant did not have possession of a genus of peptides comprising SEQ ID NO:10 at the time the invention was made.

Thus, the specification does not provide an adequate written description of a peptide comprising SEQ ID NO:10, that is required to practice the claimed invention.

REJECTION UNDER 112, FIRST PARAGRAPH, ENABLEMENT

Claims 1, 3-5 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

A. Claims 3-5 are rejected under 112, first paragraph, for lack of enablement for a pharmaceutical composition comprising the peptide comprising SEQ ID NO:10, which could be used as a vaccine.

Claims 3-5 are drawn to:

A pharmaceutical composition comprising a peptide comprising SEQ ID NO:10, with pharmaceutically acceptable excipients (claim 3),

A composition of claim 3, further comprising one or more peptides binding MHC class I molecules corresponding to CTL CD8+ epitopes (claim 4), and

A composition of claim 3 for use as a vaccine (claim 5).

It is noted that inherent in a pharmaceutical composition is the in vivo use of. The specification discloses that :

1) A pool of MAGE-3 peptides , SEQ ID NO:10 (amino acids 171-185), together with SEQ ID NO:3, stimulates proliferation of CD4+ cells from PBMC of healthy donor (Example 3 on pages 13-15, and figure 1), wherein the CD4+ T cells predominantly recognize SEQ ID NO:10 (p.14, lines 29-32 and figure 1C) .

2) MAGE-3 specific CD4+ T cells from a melanoma patient recognize SEQ ID NO:10 (p.15, lines 17-26).

3) Concerning cytotoxicity, CD4+ T cells could lyse lymphoblastoid cell line (LCL) pulsed with SEQ ID NO:10 (figure 3A).

4) The CD4+ T cells could lyse melanoma cell lines OI TC and MD TC, wherein the lytic activity is inhibited by the addition of LCL lymphoblastoid cell line pulsed with peptide 281-295 (SEQ ID NO:10), thus demonstrating that this sequence is presented by HLA-DR11 on melanoma cell line OI TC, and that peptide 281-295 (SEQ ID NO:10) is naturally processed and forms a cytotoxic CD4+ T cell epitope (p.16, last paragraph, bridging p.17, and figure 2, 3B).

One cannot extrapolate the teaching in the specification to the enablement of the claims. Although CD4+ T cells could recognize melanoma cells in melanoma patients, it does not mean that the CD4+ T cells produced are therapeutic, as evidenced by the fact that the patients still have melanoma. One cannot predict that SEQ ID NO:10 would be useful for treating melanoma cells for the following reasons:

1) It is well known in the art that cancer cells could down regulate the expression of tumor antigens. White et al, 2001, Ann Rev Med, 52: 125-145, teach that antigen internalization or downregulation can cause repeat dosing to be unsuccessful due to the disappearance of the antibody target (p.126, paragraph before last). Cheever et al, PN=5,726,023, column 9, first paragraph, teach that the expression of Her-2/Neu, that is originally expressed with initiation of a tumor, could be subsequently lost, because an effective autochothonuous immune response can convert a Her-2/Neu positive tumor to Her-2/Neu negative.

2) Further cancer treatment is unpredictable. Boon (Adv Can Res, 1992, 58:177-210) teaches that for active immunization in human patients we have to stimulate immune defenses of organisms that have often carried a large tumor burden. Establishment of **immune tolerance** may therefore have occurred and it may prevent immunization and several lines of evidence suggest that large tumor burdens can tolerize or at least depress the capability to respond against the tumor (p. 206, para 2). In addition, **Boon teaches even if activated CTLs are significantly increased, the therapeutic success remains unpredictable due to inconsistencies in antigen expression or presentation by tumor cells** (p.178, paragraph before last paragraph).

In addition, Kirkin et al, 1998, APMIS, 106 : 665-679, review several melanoma-associated antigens, including NY-ESO1, and conclude that initiation of a strong immune response in vivo is an extremely rare event (p.674, first column, last paragraph). Kirkin et al teach that for some antigens, due to the existence of self-tolerance, only T cells with low affinity T-cell receptors are produced (abstract). Kirkin et al teach that although several peptides of melanoma associated antigens have been identified as recognized by CTL in vitro, and peptides from MAGE-A1 and MAGE-A3 have been tested for their ability to induce anti-melanoma immune response in vivo, only one of the peptides, peptide EVDPIGHLY of MAGE-A3, has limited anti-tumor activity, indicating their low immunogenicity (p.666, second column, second paragraph, last 6 lines). Further, even this peptide EVDPIGHLY of MAGE-A3 produces a very low level of CTL response which is detectable only by a very sensitive method, as taught by Chaux et al, Int J Cancer, 1998, 77: 538-542, abstract. Chaux et al further teach some of the CTLs have an affinity that is too low for the recognition of cells that have processed the antigen, which is different from the in vitro conditions in which the synthetic peptides are in high number when incubated with the cells (p.541, second column, second paragraph). Similarly Sherman, LA et al, 1998, Critical reviews in Immunol, 18(1-2): 47-54 teach that self-tolerance may eliminate T cells that are capable of recognizing these epitopes with high avidity . In other words, only CTLs with low affinity are left, which may not be effective for tumor treatment *in vivo*. Smith RT, 1994, Clin Immunol, 41(4): 841-849, teaches that antigen overload, due to antigen shedding by actively growing tumor, could block specifically either cytotoxic or proliferative

responses of tumor specific T cells (p. 847, last paragraph bridging p.848 and p.848). Smith further teaches that many tumors progressively lose MHC representation at the surface of the cell, and the loss of surface Class I MHC could severely limits the possibilities for cytotoxic T cells specific for a tumor specific antigen to find said tumor specfic antigen in the necessary MHC context (p.484).

3) Further, the specification provides no exemplification of or guidance on how to use the claimed vaccine formulation or antigen for active immunotherapy in humans. The goal of tumor vaccination is the induction of tumor immunity to prevent tumor recurrence and to eliminate residual disease. However, Ezzell (J. NIH Res, 1995, 7:46-49) reviews the current thinking in cancer vaccines and states that tumor immunologists are reluctant to place bets on which cancer vaccine approach will prove effective in the long run (see the entire document, particularly last paragraph) and further states that no one is very optimistic that a single peptide will trigger an immune response strong enough to eradicate tumors or even to prevent the later growth of micrometastases among patients whose tumors have been surgically removed or killed by radiation or chemotherapy (p 48, para 6). In addition, Spitler (Cancer Biotherapy, 1995, 10:1-3) recognizes the lack of predictability of the nature of the art when she states that "Ask practicing oncologists what they think about cancer vaccines and you're likely to get the following response: "cancer vaccines don't work". Ask a venture capitalist or the director of product development at a large pharmaceutical company and you're likely to get the same response." (p 1, para 1).

In view of the above, it would be undue experimentation for one of skill in the art to practice the claimed invention.

B. If Applicant could overcome the above 112, first paragraph rejections, Claims 1, 3-5 are still rejected under 112, first paragraph, because while enabling for a peptide sequence consisting of SEQ ID NO:10, the specification is not reasonably enabled for a peptide comprising SEQ ID NO:10.

Claims 1, 3-5 are drawn to:

Peptide binding MHC class II molecule, SEQ ID NO:10 (claim 1),

A pharmaceutical composition comprising said peptide with pharmaceutically acceptable excipients (claim 3),

A composition of claim 3, further comprising one or more peptides binding MHC class I molecules corresponding to CTL CD8+ epitopes (claim 4), and

A composition of claim 3 for use as a vaccine (claim 5).

For the purpose of compact prosecution, it is assumed that claim 1 is drawn to a peptide binding MHC molecule "comprising" SEQ ID No:10.

It is noted only the elected species SEQ ID NO:10 is examined here.

Claims 1, 3-5 encompass unknown peptide sequences attached to SEQ ID NO:10.

The specification discloses that the peptide of SEQ ID NO:10 (amino acids 282-295) is from MAGE-3 (Example 3 on page 13).

One cannot extrapolate the teaching in the specification to the scope of the claims because one cannot predict that the peptide comprising SEQ ID NO:10 would have properties related to that of MAGE-3.

One cannot predict how the additional sequences would affect intracellular processing of the polypeptides encoded by the claimed nucleic acid molecules. It is well known in the art that the ability of intracellular processing of a polypeptide by proteasomes to peptides to be presented to the MHC molecules depends on the structure and stability of said polypeptide (Kirkin et al, 1998, supra, p.673, second column, second paragraph). Kirkin et al teach that "in order to be presented to the MHC molecules, intracellular antigens should undergo several steps of antigen processing, and that important steps in this process are ubiquitination of the denatured protein followed by proteolytic cleavage of the polypeptide chain in proteasomes". Kirkin further teach that "high stability of the structure reduces the denaturation of the protein and thus ubiquitination as a degradation signal". In addition, Kirkin et al teach that "in order to gain acess to the inner proteolytic component of the barrel-shaped proteasome, the polypeptide has to be unfolded, and that the efficiency of this energy-requiring unfolding should depend on the protein structure, alpha-helical conformation is known to provide the optimal geometry for maximal amount of strength of the hydrogen bonds formed". Thus based on the teaching in the art and in the specification, one cannot predict how the sequences added to SEQ ID NO:10 would affect intracellular processing of the polypeptides. Applicant however has not taught how to make the claimed molecules

such that the polypeptides could be processed intracellularly to a peptide that binds MHC class II molecule.

Further, it is well known in the art that even a single amino acid substitution or what appears to be an inconsequential chemical modification will often dramatically affect the biological activity and characteristic of a protein, and that protein chemistry is probably one of the most unpredictable areas of biotechnology. For example, Bowie et al (Science, 1990, 257 : 1306-1310) teach that an amino acid sequence encodes a message that determine the shape and function of a protein and that it is the ability of these proteins to fold into unique three-dimensional structures that allows them to function and carry out the instruction of the genome and further teaches that the problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex (col.1, p.1306). Bowie et al further teach that while it is known that many amino acid substitutions are possible in any given protein, the position within the protein's sequence where such amino acid substitution can be made with a reasonable expectation of maintaining function are limited. Certain positions in the sequence are critical to the three dimensional structure/function relationship and these regions can tolerate only conservative substitutions or no substitutions (col.2, p.1306). The sensitivity of proteins to alterations of even a single amino acid in a sequence are exemplified by Burgess et al, (Journal of Cell Biology, 1990, 11: 2129-2138), who teach that replacement of a single lysine residue at position 118 of acidic fibroblast growth factor by glutamic acid led to the substantial loss of heparin binding, receptor binding

and biological activity of the protein. In transforming growth factor alpha, replacement of aspartic acid at position 47 with alanine or asparagine did not affect biological activity while replacement with serine or glutamic acid sharply reduced the biological activity of the mitogen (Lazar et al. Molecular and Cell Biology, 1988, 8: 1247-1252). Similarly, it has been shown that aglycosylation of antibodies reduces the resistance of the antibodies to proteolytic degradation, while CH2 deletions increase the binding affinity of the antibodies (see Tao. et al. The Journal of Immunology, 1989, 143(8): 2595-2601, and Gillies et al. Human Antibodies and Hybridomas, 1990, 1(1): 47-54). These references demonstrate that even a single amino acid substitution or what appears to be an inconsequential chemical modification will often dramatically affect the biological activity and characteristic of a protein.

The specification does not disclose how to make the claimed peptide comprising SEQ ID NO:10, such that they would function or have the properties as claimed.

In view of the above, it would be undue experimentation for one of skill in the art to practice the claimed invention.

REJECTION UNDER 35 USC 102(e)

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant

for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claim 1 is rejected under 35 U.S.C. 102(e) as being anticipated by US 5,965,535.

Claim 1 is drawn to peptide binding MHC class II molecule, SEQ ID NO:10.

For the purpose of compact prosecution, it is assumed that claim 1 is drawn to a peptide binding MHC molecule "comprising" SEQ ID No:10.

It is noted only the elected species SEQ ID NO:10 is examined here.

US patent 5,965535 teaches a MAGE-3 sequence of 314 amino acid, which comprises SEQ ID No:10, as shown by MPSRCH sequence similarity search (MPSRCH search report, 2004, us-09-914-239-(10).std.rai, pages 1-2, of record).

REJECTION UNDER 35 USC 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 3, 5 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 5,965,535, supra, in view of Johnstone and Thorpe (Immunochemistry in Practice, 2nd Ed., 1987, Blackwell Scientific Publications, Oxford, pages 49-50).

Claims 3, 5 are drawn to:

A pharmaceutical composition comprising the peptide of claim 1, with pharmaceutically acceptable excipients (claim 3),

A composition of claim 3 for use as a vaccine (claim 5).

It is noted that a pharmaceutically acceptable carrier could be interpreted as any type of carrier, such as buffer, provided that it is pharmaceutically acceptable.

It is further noted that Claims 3, 5 recite the claimed peptide comprising SEQ ID NO:10, formulated as a pharmaceutical composition, or for use as a vaccine. However, this limitation is viewed as a recitation of intended use and therefore is not given patentable weight in comparing the claims with the prior art. Claims 3,5 read on the ingredient per se, which is a peptide comprising SEQ ID NO:10 in a pharmaceutically acceptable carrier.

The teaching of US 5,965,535 has been set forth above. US 5,965,535, however, does not teach a pharmaceutically acceptable carrier.

Johnstone and Thorpe teach that compositions of antibodies are stored in phosphate buffer saline, which is considered to be an acceptable carrier for storage of antibodies, because Johnstone and Thorpe teach that antibodies could be damaged,

even though antibodies are robust proteins, and that antibodies are happiest in neutral isotonic buffers such as PBS (p.50, first paragraph).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to store the sequence taught by US 5,965,535 in buffer, such as phosphate buffer saline (PBS), because of the following reasons: 1) Johnstone and Thorpe teach that compositions of antibodies are stored in phosphate buffer saline, which is considered to be an acceptable carrier for storage of antibodies, because Johnstone and Thorpe teach that antibodies could be damaged, even though antibodies are robust proteins, and that antibodies are happiest in neutral isotonic buffers such as PBS (p.50, first paragraph), and 2) Antibodies are proteins and it was conventional to store proteins in phosphate buffer saline. One of ordinary skill would have been motivated to do so in order to develop compositions suitable for storage. One of ordinary skill would have motivated to do so with a reasonable expectation of success.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MINH-TAM DAVIS whose telephone number is 571-272-0830. The examiner can normally be reached on 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, JEFFREY SIEW can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

MINH TAM DAVIS

April 13, 2005

SUSAN UNGAR, PH.D
PRIMARY EXAMINER